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Chronic Obstructive Pulmonary Disease

J. Richard Bumgarner and Frank E. Speizer

Chronic obstructive lung (pulmonary) disease refers to several disease manifestations and is known by many names—cor pulmonale (heart disease with an underlying pulmonary deficiency), right-sided heart disease, asthma, emphysema, chronic bronchitis, and peripheral airways disease are among the most common. Often these names refer to one or another of the pathological manifestations which are here grouped as chronic obstructive pulmonary disease (COPD) and its allied conditions. The many and varied names indicate in part the uncertainty in the clinical diagnoses of these conditions as well as the fact that the respiratory tract has a limited number of ways to respond to injury: the obstructive pattern is the unifying manifestation of these conditions.

Description of the Diseases

Because all the conditions of COPD are characterized by airways obstruction, the clinical manifestations and definitions overlap considerably, and diagnosis and measurement of their progression have not in the past, unfortunately, been obtained in a uniform manner.[1] For example, *chronic bronchitis* involves inflammation and narrowing of the large bronchial passageways to the lung. It is accompanied by severe coughing caused by the hypersecretion of mucus in the inflamed passages. The cough sounds terrible and is discomforting to the patient, but in itself it is seldom seriously disabling. The condition is not normally fatal, providing there is good access to medical care to control primary inflammation and to avoid the consequences of secondary infection. Usually the condition abates when the cause of the inflammation is removed. Clinical information about this condition is usually obtained from a standard set of questions about cough and sputum production. *Emphysema* is best characterized by a history of shortness of breath resulting from progressive destruction of lung tissue. In sequence there is a loss of elastic structure followed by the destruction of alveolar walls and the collapse of smaller airways. This eventually results in the loss of ability to transport oxygen from the airways to the blood and the reduced rate of exchange of carbon dioxide from the blood to the airways. This change in diffusion may eventually affect the heart, leading to right-sided heart failure. There is no cure for emphysema—once tissues have been degraded the loss of ventilatory function is irreversible. Diagnosis is normally accomplished through measurements of abnormally premature and permanent declines in lung function, but clinical confirmation has been dependent upon the pathologic examination of lung tissue, generally obtained by autopsy. Newer, but expensive, imaging techniques—computerized tomography (CT) scanning—now make it possible to confirm diagnosis of emphysema while the patient is alive. *Cor pulmonale* is characterized by clinical evidence of right-sided heart failure with edema (fluid retention in the limbs). This condition is generally superimposed on severe obstructive airways disease and long-standing respiratory insufficiency with hypoxia and hypercapnia. *Chronic obstructive lung disease not otherwise specified*, more recently reported in many health systems, generally means irreversible obstructive disease by physiologic testing but does not specify the type of disease. A great deal of this disease category is probably chronic bronchitis with obstruction or emphysema. Collectively, these diseases are referred to here as COPD.

Persons suffering from one or more manifestations of COPD have abnormally rapid rates of decline in lung function to levels which are severely disabling by middle life and fatal in severe cases. In addition, COPD contributes to the severity and eventual fatal outcome of cardiovascular diseases, including coronary and rheumatic heart disease, and other respiratory diseases, such as pneumonia and pulmonary tuberculosis.

Other diseases affect and can also complicate declines in respiratory function. *Asthma* is induced by a wide variety of allergic and nonallergic agents and produces widespread inflammation and narrowing of the airways. It is characterized by a history of recurrent episodes of wheeze, with or without shortness of breath, but with reversible airways obstruction. Its onset can be sudden and severe. Treatment with bronchodilators or anti-inflammatory agents can provide rapid return of normal lung function. In many patients lifestyle and productivity remains normal until the next episode. Other pulmonary conditions, such as pneumonia, pneumoconiosis, silicosis, and byssinosis can complicate or exacerbate underlying COPD. These diseases, however, are distinct from COPD.

Etiology of COPD

The pathogenesis of COPD is not yet fully understood. Two main mechanisms have been postulated (airflow obstruction and mucus hypersecretion), and these are believed to be independent but overlapping disease processes (Peto and others 1983). First, airflow obstruction can be caused by the presence of excessive amounts of elastase, an enzyme that is responsible for degrading elastin in the lung and destroying alveolar walls, resulting in emphysema. The absence of alpha$_1$-antiprotease, a protein that acts as an elastase inhibitor, is one genetic model for the occurrence of emphysema. In addition, it is known that the inhalation of particulates in smoke results in an inflammatory response in the lung, which increases production of elastase. At the same time, it has been shown that cigarette smoke acts by oxidizing alpha$_1$-antiprotease, resulting in the removal of the natural control on elastase production (U.S. Surgeon General 1984). These processes and other unknown enzymatic processes may interact and lead to the resulting destruction of lung tissue and the condition of emphysema.

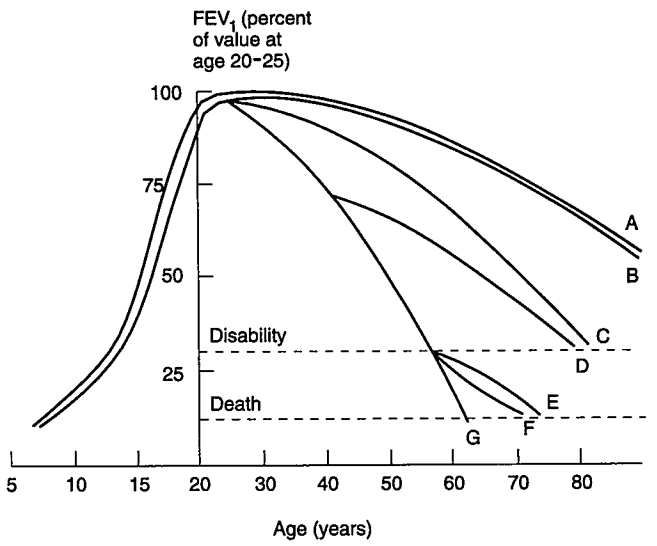
Second, the muco-ciliary apparatus of the respiratory tract is a natural defense against particulate matter which may be inhaled. The cilia, tiny hairlike projections, are coated with a thin layer of mucus that envelops entering foreign particles. The cilia beat in waves about 1,000 to 1,500 times each minute, propelling foreign particles upward to the trachea. Many pollutants, including cigarette smoke, cause transient paralysis of the cilia. Over a long period, the cilia may be permanently injured by such pollutants. In addition, chronic irritation increases production of mucus by the bronchial mucus glands. The thick, excess mucus not only overwhelms the cilia but may also plug the bronchioles, resulting in the development of chronic bronchitis with recurrent lower respiratory tract infections and increased morbidity from airways obstruction (Carnow and others 1970). Protection of the alveoli from the particular matter and pollutants is consequently reduced, and production of elastase and greater oxidization of alpha$_1$-antiprotease is likely to be increased.

Lung Function and the Development of COPD

Lung function can be clinically measured and recorded as various indexes of the ability of the lungs to take in and expel air. A simple physiologic test is performed by having patients take as big a breath as they can and blow out as fast and as hard as they can into a recording device (a spirometer) that measures the volume of air expelled in a specified time. The forced expiratory volume in 1 second (FEV$_1$) is a common measure. By comparing the FEV1 of individuals with standards measured in large population groups and adjusting for body size (height or height squared) and age for each individual, one can calculate a percent-predicted (percentage of norm) value for FEV1. Because no single study has been able to follow a population from early adult life on into the development of COPD in mid-life to late mid-life, investigators have relied upon relatively short-term prospective studies of several years to piece together the approximate natural history of lung function in a healthy individual. They have found that it increases with age until about the mid-twenties, when it begins a slow, natural decline. The lungs have a large ventilatory reserve, and the decline does not normally become evident as a significant limit on lifestyle or work capacity (curve A; see figure 24-1). Most persons who fall between 35 percent and 50 percent of the predicted value of FEV1 become short of breath on minimal exertion, and to a variable degree this may lead to a complaint to their health care provider. Because decreases of function to this level generally occur only gradually, the definition of the onset of disease, when such a complaint is made, is also variable. This is in sharp contrast to the definition of onset of a myocardial infarction or the diagnosis of a cancer. For COPD it is thus difficult to define the transition between health and disease.

Only a relatively small group (approximately 20 percent) of the population (mostly, but not all, smokers) reach a level of lung function associated with disability. The remaining nonsmokers and smokers simply do not live long enough to become disabled from lowered levels of lung function. Smokers whose rate of decline of lung function is rapid and who stop smoking in early mid-life do not regain a substantial amount of lung function, but their rate of loss becomes more like that of a nonsmoker (curve D and/or curve E in figure 24-1); if they stop smoking soon enough they may not reach the disabling level of lung function in a normal lifetime. This does not mean that such a smoker will be protected from the other ravages of smoking.

Figure 24-1. Theoretical Curve Representing Varying Rates of Change in FEV by Age



Note: Curve A represents normal decline in FEV$_1$. Curve B shows less than optimal development of normal lung function. Often, the disability-related decline continues as a variable rate curve (C). Curve D shows effect of smoking cessation; also seen in disabled individuals (curve E). Curve F is a disability-related decline continuing at variable rate. Curve G represents the accelerating decline in FEV$_1$ with cigarette smoking and continuing rapid decline until death as a consequence of respiratory failure.
Source: Speizer and Tager 1979.

For those patients who do become disabled and do not give up smoking, COPD is a devastating disease that often kills in less than five years. Death from respiratory insufficiency would occur at about FEV1 at 15–25 percent of predicted value. Even before being disabled those subjects with lower levels of lung function at approximately age forty-five have almost a fifty-fold higher risk of mortality in a twenty-year period (Peto and others 1983) than subjects whose level of function is better than average.

Maximal lung capacity is different for each individual. One question of current research interest in the industrial world is how to identify which persons, and in particular which smokers, are at greatest risk of developing COPD. Authors of longitudinal studies in children have observed a high degree of tracking of lung function, leading to the suggestion that risk factors that put children on tracks of lower growth rate of lung function, such that these children never quite reach their maximum predicted level of lung function in early adult life, may explain those persons with more decline in lung function. Factors that reduce the rate of lung growth in children are discussed below.

Risk Factors

The main risk factors for COPD are several and diverse.

Cigarette Smoking

The best-documented cause-and-effect relationship in the etiology of COPD is cigarette smoking (Palmer 1954; U.S. Surgeon General 1984). Numerous studies have confirmed cigarette smoking as a primary cause of COPD. There is a clear dose-response relationship between the prevalence of chronic mucus hypersecretion and obstructive airways disease and the quantity of cigarettes smoked (Anderson, Ferris, and Zickmantel 1964; Ferris 1973). Prospective studies in a number of countries show much higher COPD mortality in smokers than in nonsmokers. The onset of symptoms associated with COPD may occur at an early age and at relatively low levels of cigarette smoking (Peters and Ferris 1967).

Individual Susceptibility

Individual susceptibility must play a role and the multiple factors involved are not yet fully understood. A hereditary cause of emphysema was first described by Eriksson (1965). A deficiency in alpha$_1$-antiprotease is a recessive genetic trait that in its severest form predisposes subjects to the development of emphysema even without exposure to cigarette smoke.[2] Those who are heterozygote for the putative gene appear to be more susceptible to cigarette smoke. Fortunately the gene frequency of this condition is relatively low, and the condition cannot account for more than a few percentage points of the total number of cases of emphysema. Other familial factors include increased frequency of allergies, possibly associated with increased airways responsiveness, and possibly with common indoor environmental exposures. The roles and importance of these factors are unknown at present.

Air Pollution

Both indoor and outdoor air pollution have long been recognized to be potentially exacerbating factors for COPD. Illness in patients with preexisting disease symptoms clearly worsened in association with daily changes in peak levels of smoke (Lawther 1970), and overall levels of air pollution have been recognized to have a short-term acute effect on persons with the disease. During dramatic episodes of air stagnation and pollution in London, New York, Japan, and Dublin, substantial excess mortality occurred among the elderly and in those with preexisting disease who were exposed to the high concentrations of smoke and sulfur dioxide (Holland 1983). The morbidity resulting from short-term exposure could not distinctly be attributed to pollution rather than adverse meteorological (cold temperature and high moisture) conditions.

The causal role of air pollution in COPD has been examined in several British studies done in the 1950s and 1960s (such as Holland and Reid 1965; Holland and others 1965). Both these and American studies (Reid and others 1964; Deane, Goldsmith, and Quma 1965; Wynder, Lemon, and Mantel 1965; Densen and others 1967) have to date failed to demonstrate conclusively a causal link between air pollution and the onset of COPD. Conversely, smoking behavior alone has not been sufficient to explain the geographic differences in the prevalence of symptoms in England (Lambert and Reid 1970). Prevalence rates for symptoms were found to increase with increasing levels of air pollution independently of cigarette consumption, indicating that atmospheric and indoor smoke pollution may account for the urban-rural differences in the data on respiratory morbidity in Britain (Reid and Fairbairn 1958).

In developing countries also COPD appears to be unexplainable solely by cigarette smoking, because mortality and prevalence rates often appear to be much higher than in industrial countries and to have more equal sex ratios. For example, the frequency of chronic bronchitis in northern India would appear to be explainable by tobacco use among men, but its prevalence in women may be indicative of the effect of chronic exposure to fumes produced during cooking with cow dung, wood, and coal (Malik 1977). In a study of nonspecific lung disease in Delhi in which similar studies in London and Chicago were compared, Saha and Jain (1970) found that 16 percent of Delhi patients were nonsmokers, whereas nearly all patients in the other two studies were smokers. In addition, cigarette smoking and occupational air pollution (including exposure to steel, coal, cotton, and other dust) act additively in causing chronic lung disease (Commission of the European Communities 1975). Exposure to multiple risk factors in developing countries may be much higher than in industrial countries, and the effect of these multiple exposures has not been fully evaluated.

Childhood Respiratory Tract Infections

Samet, Tager, and Speizer (1983) reviewed suggestive but not conclusive evidence on the relationship between lower respiratory tract infections in childhood and the subsequent development of COPD. Respiratory illness in early childhood has been shown to be associated with lower levels of lung function in children six to ten years old (Tager 1983; Gold 1989). Among Chinese children, passive exposure to cigarette smoke from fathers who smoked nearly doubled the relative risk of severe respiratory infection in the first eighteen months of life (Chen 1986). Studies in Papua New Guinea, where from birth people are exposed to wood smoke in unventilated huts, show high rates of respiratory infection and chronic bronchitis (Colley and Reid 1970). Other studies support the notion that respiratory disorders in children predispose them to later disease (Cooreman and others 1990); and in general, children's lung function tracks uniformly from early childhood (Dockery 1983). As shown on curves A and B in figure 24-1, lower lung function in early adult life would be anticipated to result from impaired respiratory functions in childhood. The effect of this reduced maximally attained lung function may determine the plateau from which further declines during adulthood can be expected. This hypothesis remains unconfirmed, however, because no studies have yet followed individuals long enough to determine whether it is the effects of cigarette smoking or other factors that put those who have slightly lower lung function by early adulthood at greater risk of developing COPD in later life.

Occupational Dust Exposure

Becklake (1988) and other researchers have documented an association between other specific and nonspecific occupational dust exposure and excess chronic mucus hypersecretion and obstructive airways disease. Dust exposure appears to exacerbate (but not cause) COPD, and the effects can often be managed by improved ventilation or protective respirator equipment use at work.

Socioeconomic Status

Low socioeconomic status may be a surrogate factor for a number of less fully understood risk factors for the development of COPD and has been investigated in a number of studies (Colley and Reid [1970] list many studies). Factors may include higher prevalence of cigarette smoking, poorer nutrition, higher levels of indoor smoke exposure, and poor housing conditions, all associated with increases in the frequency of other respiratory illnesses, occupational exposure, difficulties in reaching health care services, and less contact with health education. Rapidly changing external and domestic factors have made long-term cohort studies among such groups difficult and expensive to conduct. Firm conclusions related to these associations remain few even after more than two decades of work relating to these questions.

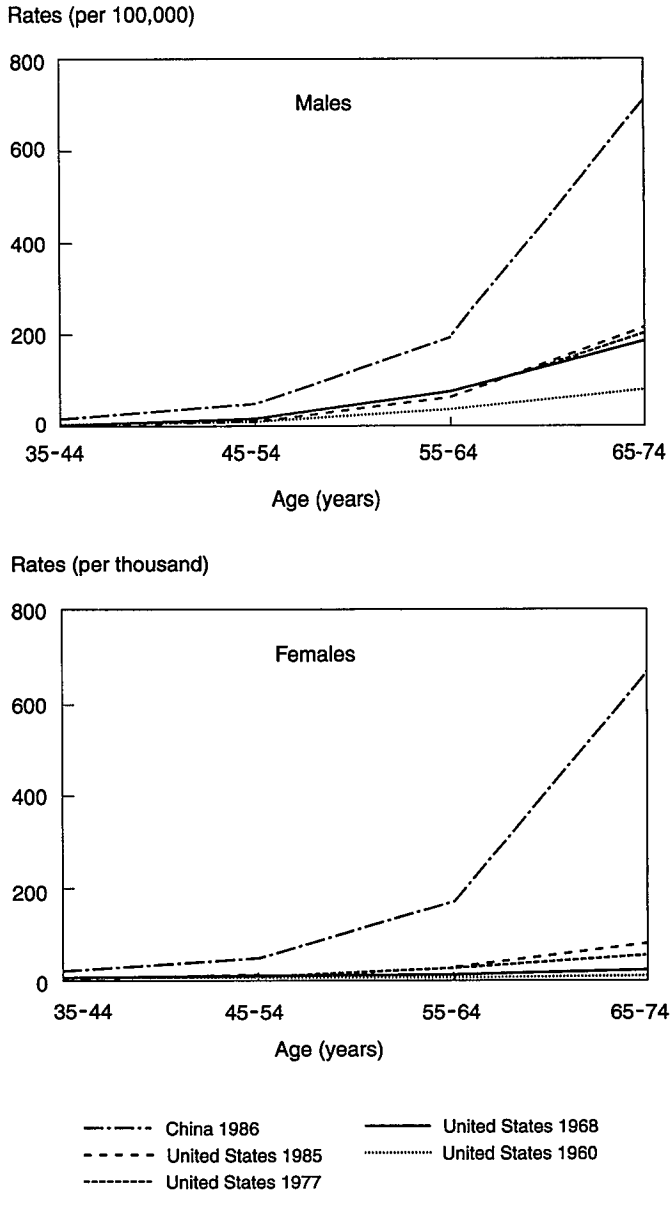
The Public Health Significance of the Condition

From an epidemiological perspective COPD must rank as a major public health problem.

Mortality and Morbidity

Death from COPD as the primary cause can occur directly because of respiratory failure or because of right-sided heart failure. Mortality rates from COPD in many industrial countries have consistently been higher for men than for women because of the longer and heavier smoking experience among men.

Figure 24-2. Age-Specific Mortality Rates for COPD in United States and China, by Sex



Source: National Center for Health Statistics for United States; Disease Surveillance Points, Ministry of Public Health, for China.

Death rates from COPD for women are increasing more rapidly than for men in the United States as the effect of more widespread cigarette smoking among women is becoming evident. This trend is substantiated by changes in female mortality from lung cancer, now the leading cause of cancer death among U.S. women. Total deaths in the United States from COPD have more than doubled from 30,000 in 1970 to more than 71,000 in 1986, with increases for each age group (figure 24-2). The corresponding male-to-female ratio declined from 4.3:1 to 1.8:1. Indirectly, COPD contributes to death from a wide variety of other conditions, including most particularly cardiovascular diseases and infectious pulmonary diseases. In many places death reports do not specify contributory causes reliably, and it is very difficult to estimate the true overall mortality contribution of COPD. In the United States, COPD is estimated to be a contributing cause of death about 1.7 times as often as it is a primary cause (U.S. Surgeon General 1984). Because of the silent, progressive nature of the disease, much underlying morbidity is never discovered or reported. In the United States, COPD morbidity is estimated at about 10 times direct COPD mortality, and many patients suffer illness and disability for many years before death (U.S. Surgeon General 1984). This hidden morbidity burden may be even larger in developing countries in which health care contacts are few.

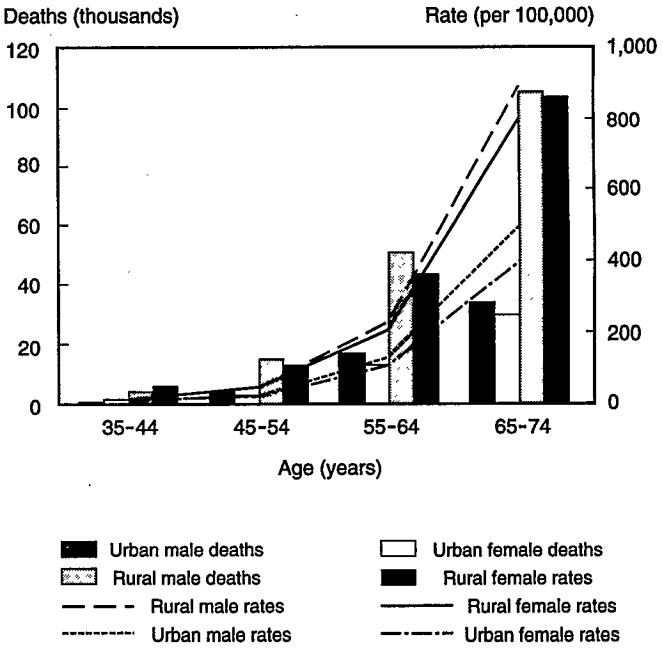
Availability of good prevalence and incidence data for COPD in most countries is seriously hampered by a lack of consistency in reporting. The disease has been redefined and reclassified frequently under the international classification systems. Inconsistency and weaknesses in recording of underlying causes of death in most countries further mask COPD's contributory effect and the disability burden which the disease poses. In the developing world COPD has been little studied and does not rank high on the public health agenda. Yet both relatively and absolutely, it is certainly a more important cause of death and illness in the developing countries than in industrial nations.

Current Levels and Trends in the Developing World

Data on COPD for the developing world is scarce. Cor pulmonale accounted for 20 percent of hospital admissions, evenly distributed between the sexes, for heart disease in Delhi, India (Pahmavati 1958). Studies in India have shown chronic bronchitis prevalence to be between 1.5 and 12 percent, and similar figures have been reported for other parts of the world. In Nepal, prevalence rates for chronic bronchitis (about 18 percent male; 19 percent female) are close to parity, and a hospital survey found prevalence of emphysema and cor pulmonale to be 3 percent and 1.5 percent, respectively (Pandey 1984a and 1984b). Nepalese data also indicate significant morbidity burdens. Among 39,000 inpatient admissions, COPD-type diseases accounted for 5.4 percent in 1984. Among 127,000 health post visits by patients (fifteen posts, Kaski district), 3.4 percent of the illnesses were bronchitis, emphysema, and asthma. In the 210,000 population served by these health posts, these diseases, at a rate of 60 per 100,000, were the third leading cause of death in 1985 (Nepal: His Majesty's Government/WHO 1987). Very limited data from the annual health survey of Pakistan show nonspecific respiratory disease accounting for about 5 percent of total morbidity. Jamaica reported death rates from bronchitis, asthma, and emphysema of only 8 to 9 per 100,000 in the early 1980s (USAID 1987). In Bangladesh in 1975–78, these disease categories accounted for 2 percent of total mortality. In Indonesia, COPD was the third ranked cause of death in the age group forty-five through fifty-four, and the main killer in the age group over fifty-five (Indonesia 1984). Review of epidemiological information from a number of African countries also points to relatively high prevalence of COPD and to the primary need for prevalence surveys with consistent criteria and methodology to establish better baseline data (Chaulet 1989).

Detailed data from China on cause of death provide the best perspective of COPD epidemiology from a developing country.[3] These data indicate that progressively higher age-specific rates prevail just as they do in the industrial nations (figure 24-3) and at rates which are much higher than even in the United States (figure 24-2). Other data reported by China in 1989 to the World Health Organization (WHO) on death among a population of 100 million corroborate this and add evidence that COPD may be a much more serious problem for the developing world than generally recognized. In China many large-scale surveys of respiratory disease document three common manifestations of COPD (cor pulmonale, chronic bronchitis, and emphysema). Cigarette smoking is an identified primary cause in most studies, but nearly equal sex ratios, a poverty-linked gradient, and dust and smoke exposure show that other

Figure 24-3. Rates and Deaths from COPD in China, by Age, Sex, and Residences, 1986



Source: Disease Surveillance Points, Ministry of Public Health, China.

factors are at work (Yan 1989). Smoking of traditional forms of tobacco may be part of the explanation. Although no detailed data on traditional tobacco use in China are available, it is common in rural areas and among middle-aged women as well as men.[4] More detailed examination of the cause of death data from China also reveals that the high COPD rates are not simply misdiagnosed rheumatic heart disease or misclassified respiratory disease.

Whatever their cause, the high rural rates in China may signal a potentially serious development for China and perhaps for other developing countries. The prevalence of cigarette smoking in China is increasing, and the age of initiation is falling. The epidemiological effect of the spread of cigarette smoking in the last decade cannot yet be fully reflected in the data shown in the charts, and large increases in smoking-induced COPD must therefore inevitably lie ahead. Declines in chronic nonspecific respiratory illness, which China and other countries might be expected to achieve as a result of reduction of poverty, fewer respiratory infections in childhood, cleaner indoor air, and improved living standards generally, could be offset, even overwhelmed, with increased morbidity and mortality attributable to a group of smoking-related diseases, including much higher incidence of COPD.

Much of the present burden must be related to indoor and outdoor smoke exposure, poor living and nutritional conditions for some children, and childhood respiratory infections, even though today we cannot conclusively document the causal role and interaction of these factors. Indoor air pollution from soft coal, wood, and dung used for household heating and cooking has been demonstrated to cause high levels of indoor smoke pollution in the absence of adequate ventilation and chimneys and can add substantially to the level of outdoor smoke. Clifford (1972), in his study in the Kenyan highlands, estimated the exposure to (mainly indoor) airborne total suspended particulates at 25,000 milligrams per year. Similarly, Smith and others (1983) showed that women in kitchens in Gujarat, India, were inhaling levels of benzopyrene, a potent carcinogen present in cigarette smoke, equivalent to smoking twenty cigarettes a day. Although the carcinogenic effects of this smoke level may have no direct link to COPD, they are indicative of the levels of smoke which must be present in such "micro" environments. Overall, these examples strongly indicate that COPD is a much heavier burden on the poor in developing countries, and on poor women and girls in particular, than the literature has thus far generally recognized.

The Progression of COPD in Developing Countries

The prevalence of COPD in most developing countries is today only roughly known, despite the evidence summarized above that COPD is a significant cause of morbidity and death in many parts of the developing world. Data on the prevalence of COPD and its risk factors and on COPD deaths are not adequate for most countries to permit even crude quantitative estimates of the overall economic effect of COPD and the benefits of its prevention. Too little is yet known about the mix of both traditional and modern risk factors and their relative roles, other than cigarette smoking. Trends in developing countries for traditional risk factors are largely unknown. Prevalence of cigarette smoking and per capita consumption are following upward trends, sometimes sharply, as is the initiation of smoking at younger average ages.

Costs and the attributable benefit of programs for COPD prevention must remain educated guesses at best, given the absence of much better data on risk factors, disease prevalence, and case treatment. Three factors will, however, inevitably make COPD a much more important disease in the future:

- COPD is a disease which mainly strikes in middle and old age. As populations in the developing world age, the absolute number of COPD cases and deaths will increase. With regard to absolute demand for care, and in comparison with infectious and childhood diseases, COPD will become more important.
- Factors which are not well understood cause high rates of COPD in many developing countries. The longer the exposure that aging populations have to risk factors, the greater probability they have of developing disease. Conversely, prospects for reductions in these risks are uncertain at best.
- Cigarette smoking continues to increase in all parts of the developing world and probably will add to the existing age-specific rates, perhaps rapidly and substantially.

These three factors allow at least a very rough estimation of the future course and seriousness of COPD. In table 24-1 we provide an estimate of COPD mortality by major region of the world for 1985. We also show the increases by region in the number of COPD deaths which can be expected if age-specific rates remain as they are today. These increases are the result of the demographic shift that is taking place as more people live to middle and old age because they are no longer dying from infectious diseases at younger ages. This increase in COPD

Table 24-1. Estimated and Projected COPD Mortality by Region, Considering Prospective Demographic Changes Only
(thousands)

	Year		
Region	*1985*	*2000*	*2015*
Industrial market economies	205	255	316
Industrial nonmarket economies	109	150	175
Latin America and the Caribbean	18	28	43
Sub-Saharan Africa	57	90	145
Middle East and North Africa	21	33	51
Asia and the Pacific	510	788	1,155
World	926	1,328	1,954

Source: 1985 data from paper prepared for World Bank Health Priorities Review 1989; future deaths derived by using 1985 age-specific rates applied to population cohorts presented in World Bank Population Projections 1987–88.

deaths (and morbidity) that is induced by age structure will, of course, be more pronounced in those areas of the world where present-day societies are mainly young and the number of middle-aged and old persons will grow sharply in the next thirty 30 years. The industrial countries are least affected by changes in age structure as these have already largely taken place. Overall there may be more than a doubling of COPD mortality in the developing world.

The second factor which will influence future COPD incidence and mortality is exposure to risk factors. It is clear that there are multiple risk factors for COPD in the developing countries, which can be only poorly documented or explained. These include early childhood respiratory infection, exposure to indoor smoke, air pollution, occupational dust exposure, and others. It is at least a plausible hypothesis that some of these risks will decline in time with general economic improvement, better access to primary health care, improved housing and living conditions, better nutrition, and other changes. Factors such as these may underlie the substantial decline in COPD prevalence in Britain among nonsmokers in the first three-quarters of this century. It is equally plausible, however, that persistent poverty, malnutrition, inadequate health services, poor housing, and rigid social systems in poor countries will preclude early development of a declining trend in COPD prevalence.

Increased cigarette smoking in developing countries will substantially affect COPD rates, particularly among the young in Asia, who in many places are becoming early and heavy smokers. In table 24-2 we show an estimate of COPD mortality which may occur from the combined effects of an aging population and increasing age-specific death rates resulting from cigarette smoking. It is assumed in these estimates that risks associated with other (traditional) factors remain constant and do not multiply cigarette-associated risk. The estimated growth in age-specific mortality rates used to derive these numbers is similar to that experienced by smokers in the same age groups in the United States from the mid-1950s to the mid-1980s. It entails the simple assumption that similar etiological effects will be evident among large populations elsewhere who smoke.

In developing countries it is possible that age-specific rates will rise even more rapidly than they did in the United States for three reasons. First, during the latter half of the period used to derive these data, there were sizable reductions in the United States in the number of cigarettes smoked and in smoking prevalence. Similar trends may not occur in developing countries. In fact, many poor countries are experiencing rapid growth in both per capita consumption and in overall smoking prevalence. Second, the effect of increased cigarette smoking in a population with lung function already impaired by other long-standing risk factors is likely to be more severe than smoking among a relatively unimpaired population such as that of the United States. Third, to the extent that potentially offsetting improvements in living standards, health care, and so on are achieved in the developing countries during the next thirty years, the beneficial effect on COPD mortality will be limited. The irreversible nature of most COPD and the effects of impaired respiratory development and of earlier lifetime exposure mean that for most of those between the ages of fifteen and fifty today, prospective risk of COPD mortality will not diminish rapidly. The effect of reduced risk exposure to factors other than cigarettes would mainly be realized among the young and only during later periods of time, after 2015. If risk factors other than smoking do not decline in importance, or if the synergistic interaction of these risks and smoking is greater than the sum of their individual effects, then possible COPD mortality may be considerably higher than indicated in table 24-2.

The conclusion is that very early, aggressive, publicly funded programs of smoking cessation provide the only significant hope of reducing this burden for the developing world. Efforts to address the other possible risk factors may contribute to reducing future morbidity and mortality from COPD, but the strategic mix of actions and their effect is much less clear. Exactly the opposite is true for smoking—the steps and their probable effect on future COPD is quite clear.

Data to estimate present or prospective costs of the COPD illness and mortality burden for different parts of the world do not exist. In industrial countries, efforts to quantify the effect of the disease have shown its large cost. In Britain, COPD accounted for a rate of 3.7 percent of the working-age population being incapacitated for work, or about 25 percent of the total inception rate for work incapacity (Alderson 1967). A total of 300 million working days were lost annually in that country as a result of incapacitating illness lasting four or more days; this directly cost the National Insurance Fund more than £220 million (in 1965; approximately £2 billion in 1991 prices).[5] Of the total, 40 million days lost (13 percent) were attributable to COPD ("Incapacity for Work" 1966).

In the United States in 1979, COPD was estimated to cost the economy about $6.5 billion (USDHHS 1982). Of this total, about a third each was accounted for by direct treatment costs,

Table 24-2. Estimated and Projected COPD Mortality by Region, Considering both Prospective Demographic Changes and Epidemiologic Changes
(thousands)

Region	Year		
	1985	2000	2015
Industrial market economies	205	417	529
Industrial nonmarket economies	109	231	293
Latin America and the Caribbean	18	57	72
Sub-Saharan Africa	57	191	243
Middle East and North Africa	21	68	86
Asia and the Pacific	510	1,524	1,934
World	926	2,446	3,104

Note: Projections based on table 24-1 but with deaths in 2000 and 2015 adjusted to account for age-specific COPD rate increases as experienced in the United States from 1960–85.

Source: See table 17-1; World Bank Population Projections 1987–88.

indirect morbidity costs (for example, lost wages), and indirect mortality costs (premature loss of life).

In hospital studies in China, patients with cor pulmonale had one of the highest average lengths of stay (thirty-six days in a middle-size hospital; forty-six days in a large hospital), and the disease ranked in the middle of all diseases in costliness to treat per episode (535 Chinese yuan, or about US$150, in a middle-size hospital; 795 yuan, or about US$210, in a large hospital), equivalent to 48 percent and 72 percent of gross national product per capita, respectively, for each patient's hospitalization episode (Chen Jie 1986). With regard to direct costs attributable to treatment, COPD seems sure to present a large burden on already underfinanced health systems in many developing countries. The indirect economic losses due to incapacity for work and premature death are almost certain to be higher. In China, COPD is estimated to account for about 2.5 million premature years of life lost annually (3.2 percent of the total premature years of life lost). Undiscounted, this would be roughly equivalent to losses of US$750 million annually, conservatively valuing each year of life lost at average per capita gross national product (World Bank staff estimates). Much further work in health economics and accounting needs to be done to quantify better the effect and costs of COPD, particularly losses and costs resulting from morbidity, to give public health leaders the facts they need to devise and defend an effective strategy for COPD prevention and case management. It seems clear, however, that both the present and prospective costs of COPD for developing countries are much higher than commonly realized.

Lowering or Postponing Disease Incidence

Clinical studies have shown that, once lung damage has occurred, cessation of smoking can only arrest the rate of further decline. Changes in ventilatory function that have occurred to that point are essentially irreversible. There are no known studies to show whether removal of risk from indoor (noncigarette) smoke exposure or from outdoor smoke pollution has a similar, immediate, salutary effect, but it seems reasonable to assume so. Avoidance of exposure to smoke and other respiratory insults by patients suffering from ventilatory decline has been shown to reduce acute attacks, complications, and premature death.

Elements of a Preventive Strategy

The long incubation period of COPD and its silent, progressive, and irreversible nature require that prevention strategy be founded on very early, continuous primary prevention efforts. Prevention strategy must have two broad population targets: persons who do not yet have detectable signs of excess deterioration of lung function and persons who show early and moderate clinical signs of disease. Most persons in the former group will be children, young adults, and those adults who have not been long exposed to known risk. Persons in the second group will almost all be adults, most probably already in middle age (older than forty); their needs are discussed in the section entitled Case Management, below.

For the first group the strategy must aim at preventing or reducing the exposure to known and suspected risk factors. Elements of this strategy would appear to be four, in order of priority: broad and comprehensive tobacco smoking control programs; early and widespread health education programs for both the community and for primary-level health workers; a variety of investments and programs to reduce severe indoor air pollution, particularly in the home and among the poor; and limited, focused programs to reduce severe exposure to workplace or industrial air pollution. Good case management of other diseases may provide good primary prevention of COPD by the identification of children at increased risk. This can be determined by identifying children who suffer from frequent respiratory illness and who are failing in some way to grow and develop normally. Efforts need to be directed not only to caring for their respiratory illnesses but also, at a social level, to improving nutrition and reducing indoor smoke exposure—for example, by providing means to vent cooking stoves in the child's household. As the children get older and are in school, an integrated program of health education that emphasizes not smoking needs to be instituted.

Primary Prevention Strategy Elements

Because of the nature of these strategy elements, multiple agencies of government and of the community would need to be involved. In order of priority these would include the following:

- *Financial, planning, health, agriculture, industry, and commerce authorities*, who can provide the most important elements of a prevention strategy for COPD by adopting and implementing a cohesive tobacco smoking control program, probably consisting of at least the elements indicated in the next paragraph.
- *Community, religious, and other citizen groups*, which need to stimulate and cooperate with public health authorities to target women and their children who are subject to frequent respiratory infections. The range of their activities should include school, maternal and child health, family planning, and nongovernmental programs to improve childhood nutrition. Such action will build resistance to infection, a likely risk factor for impaired lung growth.
- *Urban and rural development and housing authorities*, who are responsible for, or who can influence, the design of homes and apartments to reduce indoor smoke.
- *Health authorities*, who must provide the epidemiological and professional inputs for targeting of risk groups, for continuing operational research into causes and effective interventions, and for the technical content of health education efforts.
- *Education authorities*, who must develop means and programs to ensure broad and early introduction of appropriate

health education content as the influences of "modern," especially "prosmoking," images grow.

TOBACCO SMOKING. The main risk factor for development of COPD, tobacco smoking, is common to many of the other chronic noncommunicable diseases that are important causes of mortality and morbidity in the developing world. Neither the etiology of these diseases nor the basis for a preventive strategy are well understood in many government circles. Moreover, cigarettes are often associated with governmental revenue, powerful individuals in trade and commerce, and popular images of development and sophistication and are backed by sophisticated methods of propaganda to encourage the initiation of smoking. International experience with tobacco control shows the necessity for a comprehensive, prioritized approach of tax (price) increases and legislation and regulation of access to tobacco and of its advertising. Good epidemiologic surveillance, analysis, and effective forms of health education and publicity need to be aimed at creating a social environment supportive of cessation of smoking by individuals. The overall scope of these strategy elements goes far beyond the responsibility of any single government agency in any country and requires the informed attention and action of the highest political and community leadership in each country. Tobacco control efforts also will provide one of the only country-effective primary prevention strategies for lung, larynx, oral, esophageal, bladder, pancreatic, and kidney cancers. It will substantially reduce risks of coronary heart disease, stroke, fetal mortality and spontaneous abortion, prematurity, subsequent respiratory distress syndrome death, low birth weight, and subsequent infant morbidity. The implications of tobacco control mean that this difficult topic needs to be near the top of the health policy agenda in most countries.

INDOOR SMOKE EXPOSURE. Indoor smoke exposure is related both to fuels and their price and to housing styles and familial customs and expectations. Poor persons will generally be those most necessarily reliant on the cheapest and potentially most toxic fuels (wood, soft coal briquettes, and animal dung). They will also be those who are limited to the most simple housing designs and among whom social practices may dictate additional risk—for example, lack of ventilation, attributable to beliefs that windows may allow evil spirits to enter or to efforts to ward off insects, and customs requiring that women and young children, especially girls, spend considerable time indoors, often in the rooms in which cooking or heating fires are located. Substitution of cooking gas and kerosene for powdered charcoal briquettes, dung, and wood could help to reduce indoor air pollution, but problems of expense, distribution, and adaptation of customs will surely impede widespread implementation in many countries. Simpler, and likely cheaper solutions, such as reduction of indoor smoke exposure through better ventilation, seem likely to have a more significant effect on illness and premature death in the short and medium term. Free access of girls to primary education may offer the best hope of strengthening their position in society and their capacity to bring about eventual change in social practices which put them at risk not only of respiratory illness but of other diseases and injuries as well.

OUTDOOR AIR POLLUTANTS. The less-than-clear causal link of outdoor air pollutants to chronic lung disease mediates against aggressive, expensive strategies solely on health grounds. Considerations of other aspects of environmental degradation and of other benefits from reductions in the levels of pollution will provide additional justification and perhaps contribute to better overall strategy formulation than if only COPD prevention aspects are considered. This expanded view would call for a coordinated strategy by economic, urban, housing, agricultural, forestry, educational, social, and health authorities to ensure that well-considered programs of better fuel utilization and atmospheric pollution reduction are developed. The prospects of these programs having salutary health effects are good, but the many other considerations call for a broad, multisectoral strategy.

Government programs to affect potential indoor and outdoor air pollution as a risk factor will be difficult to implement and may be costly if "alternative fuels" and housing reconstruction programs are given high priority. In conditions of poverty and restricted opportunity, resources needed for such programs may be more effectively used in other ways. Realistic strategies would seem to include concentrated antismoking efforts, coupled with well-financed health education programs to counsel nutritional, social, and behavioral changes which reduce the risk to the poor without adding to their economic burden. Social and health returns from this strategy are likely to be higher.

These efforts call for strong social and political leadership on the importance of tobacco control in the developing world together with substantial, sustained, and targeted public funding for health and social education for the poor—a goal which has proved virtually unattainable in even the richest of societies unless a national consensus is reached on the definition of problems and strong leadership effectively directs the focus of intervention. Examples are provided by earlier success in China, Sri Lanka, Kerala State in India, and in parts of Latin America with control of some endemic and infectious diseases, by the worldwide eradication of smallpox, and by the impending eradication of polio.

Case Management

The management of patients with COPD is complicated by the difficulties in defining when a subject becomes a patient. Most patients seek medical attention when they have sufficient difficulty from shortness of breath that it interferes with their activities of daily living. Persons with sedentary jobs may perceive themselves to be less affected by the disease than those who work at manual labor and may seek help later in the

development of the disease. At present the only objective measure of disease is the degree of reduction of air flow and volume from the values expected by age, sex, and stature.

Case Management Strategies

Unfortunately, by the time lung function shows excessively rapid declines, the disease generally has progressed to a point at which most of the loss of lung function is permanent and will not be recovered with treatment. This is not to say, however, that treatment is not warranted. Treatment may shorten the duration of an exacerbation of symptoms and may prevent mortality. If the patients survive, however, they are returned only to their pre-exacerbation state, and then continue on an unrelenting downward course unless the putative risk factor (most often cigarette smoking) is removed.

Because little can be offered to patients with established disease, the most cost-effective method of case management requires the finding of and intervening in the natural history of the disease at a preclinical stage with simple and relatively inexpensive procedures that require neither highly trained technical personnel nor equipment (table 24-3).

Secondary Prevention

Secondary prevention requires health care providers to begin routinely to question patients about respiratory symptoms in a standardized manner and carry out simple measures of pulmonary function to identify those subjects at greatest risk of developing disabling lung disease. Antismoking efforts and reduced occupational dust exposure must be emphasized, particularly among those subjects identified as being at risk. Medical treatment of exacerbations requires smoking cessation on the part of the patient, the forcing of fluids, and the use of a broad spectrum of antibiotics. Only if symptoms persist or worsen does the patient need to go beyond the primary provider to a facility staffed by physicians, where the same treatments with the added opportunity for bed rest and fluid administration would be available.

Rehabilitation: Management of Exacerbations

Ideally, treatment of exacerbations of COPD depend both on severity of symptoms and clinical findings and level and severity of the obstructive components of the disease. For patients

Table 24-3. Case Management, Primary and Secondary Care

	Primary care		*Secondary care*	
Objective	*Diagnosis*	*Management*	*Diagnosis*	*Management*
Secondary prevention	Positive findings of respiratory symptom questionnaire	Stop smoking	n.a.	n.a.
	Abnormally reduced lung function on simple pulmonary function testing (such as spirometry)	Reduce occupational dust exposure. Improve indoor ventilation.	n.a.	n.a.
Cure	n.a.	Cure not possible	n.a.	Cure not possible
Rehabilitation and treatment of exacerbations	Changes in symptoms (increased mucus secretion, breathlessness)	Stop smoking Administer fluids Use broad-spectrum antibiotics	Severe respiratory distress n.a.	Stop smoking Administer fluids
Maintenance care for chronic condition	Monitoring symptoms	Stop smoking	Response to bronchodilators	Trial of corticosteroids
		Improve indoor ventilation	n.a.	n.a.
	Rapid loss of pulmonary function	Breathing exercises	n.a.	n.a.
	Reduced activities of daily living			
Palliation	n.a.	None possible	Fluid retention	Home oxygen
			Severe shortness of breath	Ventilatory support in hospital only if patient has respiratory reserve
			Blood gases determination	

n.a. Not applicable.
Source: Authors.

with mild cases, removal of the inciting agent (cigarette smoking), hydration, and being kept warm may be sufficient to reduce morbidity from a given exacerbation. Antibiotics often are added to such a regime; however, the evidence is weak that they contribute substantially to shortening the duration of the exacerbation. In those patients with more severe disease, hospitalization and ventilatory support may be necessary for treatment of acute episodes. At some time during the course of severe disease patients should be given a trial of corticosteroids or at least a test of the degree of reversibility of their airways obstruction.

Because treatment has such little effect on the course of the disease the most important strategy in first dealing with patients with established disease is to remove existing risk factors. This would most certainly include requiring that the patient stop smoking; reducing or providing ventilatory protection from occupational dust and fume exposure, where possible; and reducing indoor smoke exposure.

Maintenance Care

Maintenance care is required for those patients with increasing development of disability. This can be monitored by the primary provider through evidence of increasing symptoms—"rapid" loss of pulmonary function and decreased activity in daily living. Again the treatment is to have the patient stop smoking and to teach the patient self-care strategies with breathing exercises and graded exercise training. Because a modest percentage of these patients will have or may develop a reversible component to their disease, an evaluation for reversibility should be carried out. This can be a relatively simple test of response to a bronchodilator with simple measures of pulmonary function before and after the test drug. A more formal test of response to a therapeutic trial of bronchodilator or corticosteroid lasting several weeks may be appropriate in some settings. The latter requires that the health care worker see the patient on several occasions and measure pulmonary function repeatedly.

Palliation

Palliation requires specialized treatment which in general has not been shown to have a significant effect on the course of the disease. Patients with severe fluid retention (cor pulmonale), severe shortness of breath, hypoxemia, and hypercapnia are at risk of immediate death. There are no cost-effective measures to deal with these conditions. Only life-saving treatment can be rendered, and it is only temporarily effective. Unless the prior physiologic state of lung function is known to have been at a level compatible with independent functioning, ventilatory support (up to and including assisted ventilation) is not warranted. On rare occasions in which blood gas determinations have been carried out and when local geography (for example, altitude) dictates, home use of oxygen may be required to support specific patients and may be affordable to some individuals (it cannot cost-effectively be included in public programs as long as primary and secondary prevention efforts remain underfunded). It must be stressed that these measures have no effect on the natural history of the disease but serve to keep patients comfortable and functioning for whatever time they have.

These considerations, the costs of treatment, and the long period of disablement which often accompanies COPD before death strongly mediate in favor of effective primary prevention programs with substantial public funding. In most countries it has been extremely difficult to achieve a consensus in this regard. This seems to be at least partly attributable to the complex history and characteristics and multifactorial causes of the disease. The diffuse pattern of the disease burden in the community, the socioeconomic classes most affected, and the slow progression of symptoms have added to the problem of achieving a consensus of COPD as a disease priority. With better understanding in the last decade of the causes, diagnosis, appropriate classification, and importance and effectiveness of prevention in relation to treatment alternatives, this situation may begin to change.

Chronic obstructive pulmonary disease seems to be one of the chronic diseases for which broad, well-funded, targeted, primary prevention programs and health education should be adopted by government agencies. The efforts that seem likely to be most cost-effective are those provided in the context of regular primary health care and the frequent use of widespread, nonhealth mass media (for example, newspapers, television, and radio).

Priorities

A structured approach to progress in reducing the future burden of COPD morbidity and mortality requires prioritization in several key dimensions.

Priorities for Resource Allocation

The priorities of primary prevention programs, mainly smoking control but also low-technology, low-cost interventions to reduce exposure to suspected risks, especially among the poor, should be clear from the previous discussions. The limited effectiveness and high cost of attempts at secondary prevention and treatment and cure mean that these strategies will in most countries be options only for those who are relatively well off. Public financing to deal with COPD illness will be unaffordable for most countries and, if pursued, might only increase inequities of health service provision and detract from spending which should be allocated to primary prevention.

A number of priority research activities are suggested by the current state of knowledge about COPD and its effect in the developing world. Basic research should include both epidemiology and a number of clinical and biological questions. Collection of consistent age- and sex-specific morbidity and mortality data on COPD and its course in the developing world is needed to provide a better assessment of the magnitude and trend of the problem. In addition, given the uniqueness of some

of the risks of respiratory disease to which people in developing countries are exposed, there are some questions which should be explored to investigate respiratory infection or illness as predisposing factors:

- How does nutritional status interact with the frequency, duration, and severity of acute respiratory infection in the first two years of life?
- Does the immune status (both passive and active) affect an infant's (less than two years old) or child's (age two to five) response to a viral or bacterial respiratory infection?
- What is the relation between these early life infections and eventual development of COPD?

Similar questions can be applied to other unique environmental settings—for example, in the villages in Nepal, where cold and high altitude interact with soft coal and biomass fuels to produce high levels of indoor air pollution, or in Mexico City, where altitude, weather, and high temperature interact with auto exhaust to produce high levels of ozone.

Sociobehavioral Research

Sociobehavioral research on the determinants of effective COPD health education programs (social marketing) that are focused specifically on the young, on women, and on rural populations provide another area in which research may yield important findings. Subject matter to be covered by health education could include both disease-specific information and primary prevention messages. The importance of early secondary prevention efforts can be conveyed to family members to encourage them to help those who are already at risk to take steps to stop progression of the disease. Smoking control policies provide a second important topic of research in the sociobehavioral field.

Educational Research

Educational research in both pedagogy and effectiveness of curricula for in-service training of health workers, and medical education curricula for new doctors and health workers, could include specific emphasis on the epidemiology and importance of COPD to developing countries, and on the importance of primary prevention as the basis for health care strategy. Primary school health education programs need to develop and test programs which stress healthy lifestyle practices that children can relate to in a positive way.

Priorities for Operational Research

Priorities would appear to include at least the following topics:

- Determination of the COPD risk attributable to both indoor and outdoor air pollution in developing countries
- Approximation of the attributable risk of the synergistic interaction of exposure to general smoke and to tobacco smoke, for both the smoker and the nonsmoker
- Determination of effective modes and health education messages to convey the risks and causes of COPD to different social groups in developing countries
- Cross-national epidemiologic studies to confirm and quantify better the burden which COPD poses for the poor and for women in particular

In addition, because the exposure to risk factors seems to be so high in rural areas and the population at risk is so large, it may be that the greatest marginal return to national expenditure on air pollution control will be with low-technology strategies in rural areas rather than, for example, through the purchase of high-technology emission controls for fossil-fueled power plants. In the near term, the most cost-effective means of achieving a reduction in human exposure may well be a concentration on the traditional rather than the modern sectors of the economy. Research to understand better the priorities and advantages of this strategy may yield useful insights.

These conclusions must remain speculative until further work is done, however, and this points to the overall need for much better operational research on the cost-effectiveness and cost-benefits of COPD prevention and treatment. Today we should, but cannot yet, analyze quantitatively the cost-effectiveness of alternative interventions to prevent and treat COPD. Neither can we quantify how expenditure on COPD prevention and the outcomes of it compare with the costs and effects of other health interventions. Data to permit detailed analyses of these kinds do not yet exist. We can only broadly assess some of the main factors which would determine the results of such analyses.

From an overall cost and benefit perspective, the distribution of COPD mortality among relatively older people will mean that many future potential years of life saved by COPD prevention are retirement years or the years close to them, even in developing countries. The long periods of disability preceding death which characterize COPD would mean that effective prevention and case management efforts could preserve productivity, minimize dependency, and postpone or avoid completely the expensive phases of treatment of COPD.

From a public health perspective, efforts to treat COPD seem likely to be hopelessly cost-ineffective compared with primary prevention aimed at the main known risk factors. Rehabilitation, maintenance, and palliative care for individual patients have no public health benefits. Because morbidity will already be substantial in most patients when they first seek medical attention, loss of some productivity will have already occurred, and economic benefits will thus also be limited. In comparison, early secondary prevention can arrest further morbidity, preserve productivity, and reduce or at least postpone expenditure for treatment. If conducted in a primary health care setting, opportunistic screening through simple questioning of those suspected of having COPD, followed by spirometry, should allow

rapid, low-cost finding of suitable candidates for intensive counseling, job change, house or work ventilation improvement, or bronchodilator therapy (listed in descending order of their probable cost-effectiveness).

It is less clear, however, that the cost-effectiveness of early secondary prevention would compare favorably with that of primary prevention. It seems probable that priority should be given to primary prevention for three reasons. First, most primary prevention efforts for COPD will have an effect on other chronic and communicable diseases. Second, the main risk for COPD in the future appears certain to be cigarette smoking. School and public educational campaigns and workplace and regulatory programs are known to be low cost and many have proved effective. Third, among the most effective tools for smoking reduction are taxes and fees attached to the sale of tobacco to help reduce demand for cigarettes, particularly among vulnerable low-income groups and youth. It would not be unreasonable to expect that all primary prevention efforts for smoking-related diseases could be fully funded from tobacco taxes and thus be highly cost-effective, even profitable, from a public health perspective.

Operational research in these areas to quantify better the characteristics and patterns of the costs of COPD morbidity and mortality, and the benefits of avoiding or minimizing these costs, is clearly needed and would help to establish and underpin effective programs to deal with the disease.

Notes

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1. The classification of these conditions has changed several times with revisions of the *International Classification of Diseases*. These changes reflect better understanding of the disease and its forms but make cross-national and longitudinal data analysis very difficult. Good analysis of COPD mortality and morbidity has probably been adversely affected by the classification changes and their subsequent, gradual, adoption in various national cause-of-death reporting systems.

2. The mechanism appears to be an inability to neutralize the activity of protease normally occurring in the respiratory tract.

3. The China data reported are for a 9 million population sample widely distributed across the country and are only for cor pulmonale, death from right-sided heart disease, which in the normal cause-of-death reporting for China would include most patients with long-standing respiratory insufficiency which had culminated in deterioration of the circulatory system. This category excludes tuberculosis, pneumonia, pneumoconiosis, byssinosis, and silicosis. It also excludes deaths diagnosed as respiratory disease for unspecified causes. Inclusion of these deaths would raise the reported rates by about 75 percent in most age groups.

4. Traditional tobacco smokers elsewhere are known to be at risk. In a study in rural India, "reverse chutta" smokers experienced high rates of COPD. "Reverse chutta" smoking involves consuming home-grown tobacco rolled in a semidried leaf with the lighted end inside the mouth during inhalation. Chronic bronchitis was diagnosed in 33 percent of the chutta smokers; a high, 24 percent, prevalence was found in those age thirty-one through forty years; and of those older than forty-one, a remarkable 49 percent prevalence of bronchitis was observed. Chronic airways obstruction also was found to be frequent with significant reductions in FEV1 values (Malik, Behera, and Jindal 1983).

5. A billion is 1,000 million.

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